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RECENT ADVANCES IN CHEMOTHERAPY[1]

By Dr. M. L. CROSSLEY

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Two paintings, "The Alchemical Making of a Medicine in the 16th Century," by Michael Diemer, and the "Elixer of Life" by John A. Lomax, tell an inspiring story of man's belief that from chemical investigations would result new and potent drugs capable of combating diseases and alleviating human suffering. The discoveries of the past few decades in chemistry are encouraging evidences that the alchemist's dream is being realized. Chemical compounds having no counterparts in nature have been produced and shown to be effective therapeutic agents. A beginning has been made; new and important discoveries will follow. Man may confidently look forward to a time when he will have available the means of destroying the parasitic hosts that find access to his body and conspire to destroy him.

These agents of destruction are many. They are all about man. He is always on the defensive. His life depends upon the state of his preparedness for constant chemical warfare against both plant and animal invaders. He is attacked by worms; roundworms, hookworms, pinworms, other kinds of worms; protozoa, bacteria and viruses. They would convert him into a regular British Museum of infirmities, as Mark Twain once said. They invade his intestines, his muscles and his vital organs, producing diseases which reduce his efficiency and often deprive him of life. These disease-producing organisms are the "reds" of

[1] An address before the Western Connecticut Section of the American Chemical Society, January 22, 1940.

cellular organization and like the reds in human society interpret the privilege of participating in the benefits of organization as a right to destroy what exists. The human system must fight incessantly to maintain its integrity and life.

Disease is one of the most dreaded foes of mankind. To conquer it is one of the chief aims of science. Chemistry and biology, in particular, are jointly charged with the responsibility for seeking knowledge about the diseases which menace man's health and jeopardize his life. While much progress has been made in the study of the agents causing disease, little is yet known about the exact way the causative agent works and the changes brought about in the physical and chemical activities of the cells of the tissues and organs. Also little is yet known about the nature of the chemical defense weapons of the body or of how drugs act on bacteria and other infecting agents. The knowledge of chemotherapy is still highly empirical.

The knowledge of infecting agents and the means by which they reach the human system has led to the establishment of conditions which minimize the chances of infection by them. When diseases such as typhus fever, plague and cholera were shown to be caused by microbes, the guests of vermin, sanitary engineering abolished filth in cities and eradicated vermin. The establishment of bodily cleanliness as a mark of social betterment deprived body lice of their free board and lodging and forced them to give up their human associations. Thus, man, living under such conditions, was spared the ravages of typhus fever, which was transmitted by body lice. Similarly, other insect-borne infections, causing malaria, yellow-fever, cholera and plague, have been eradicated wherever it has been possible to destroy their insect hosts. The war steadily carried on against mosquitoes has greatly improved the conditions and thus reduced the wastage of human life and relieved much suffering from malaria and yellow fever. Plague and cholera have been held in check by incessant war on the rat-flea and the bed-bug, which serve as hosts of the microbes causing the respective diseases.

The results obtained by research in the attempt to make the world safe for humanity inspire greater efforts and justify hope of success. However, to accomplish the desired results there is needed, in addition to the superlative scientific work of many investigators, a better appreciation by the public that the fight against disease is the concern of every one. People must understand the hazards to health and life by infectious agents and accept responsibility for providing conditions which will prevent the transmission of communicable diseases. The individual who sneezes in the air condemns his fellowmen to suffering and losses they should be spared. The public must learn that to treat infecting agents without restraint is to establish disease and invite the possible penalty of an early commitment to the grave for eternity.

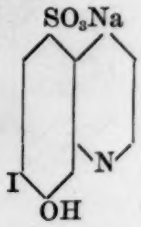
The aim of chemotherapy is to be able to treat diseases with chemical substances capable of selectively destroying disease promoting agents without doing serious injury to any vital part of the human organism. This will be difficult to accomplish. It may never be fully realized. Living organisms, simple and complex, microbe and man, possess certain characteristics shared in common by all living things. They have the capacity to assimilate, to grow and to reproduce. The cycles of events characterizing these processes in microbe and in man may involve similar phenomena. The drug which affects the protoplasm of the parasitic agent may not be wholly without toxic effect on man. If it were it would be in general ineffective as a therapeutic agent. It is a matter of degree of toxicity for each. The problem is to find chemical substances which will destroy the agents of infection, *in vivo*, in concentrations so low as to be practically harmless for the human organism.

Some progress has been made in recent years in the chemotherapy of diseases caused by both animal parasites and bacteria. However, until the recent discovery of the sulfanilamide therapy of bacterial diseases, the chief accomplishments had been in the treatment of animal parasitic diseases, particularly in the chemotherapy of amoebiasis, leishmaniasis, malaria and trypanosomiasis. To a lesser degree, progress has been made in the treatment of the diseases caused by various types of worms and flukes that invade the intestine and vital organs of man.

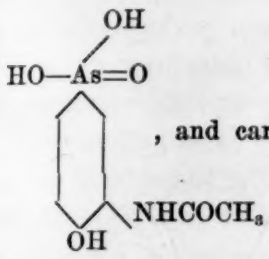
Chemical remedies for worms have been tried for a long time. Santonin and other natural drugs were used with some success. In recent years carbon tetrachloride, tetrachlorethylene and hexylresorcinol have proved to be effective remedies for certain of the intestinal parasitic infections. Thymol seems to give good results in hookworm disease. Carbon tetrachloride is said to be particularly effective against the tapeworm. However, none of these drugs is entirely satisfactory. The ideal drug for such infections is still to be discovered. Besides, there are diseases due to the filarial type of worms which are not benefitted by any of the drugs that have been investigated.

Considerable work has been done to find suitable drugs for the treatment of diseases caused by amoeba-amoebiasis. Emetin, a natural product, a derivative of iso-quinoline, has been used for a long time, but it is not satisfactory because it is a cytoplasmic poison and its effects are cumulative. Extensive investigations of quinoline and iso-quinoline derivatives have

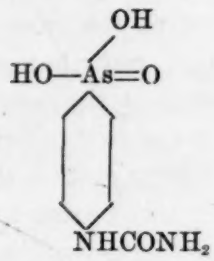
finally led to the dscovery of an iodohydroxyquinoline sulfonate, chiniofon,



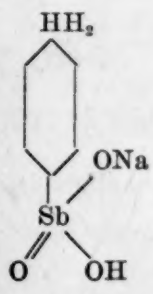
and an iodochlorohydroxyquinoline, Vioform, which have proved to be effective in amoebic dysentery. Chiniofon clears up the diarrhoea and in most cases frees the intestines from amoebae but does not appear to be effective in curing the abscesses of the intestine and liver. Vioform is claimed to be more effective but is also more toxic. Nothing definite is known of the mode of action of these drugs. Besides the quinoline derivatives some success has been had with certain organic arsenicals of the type of acetarsol,



, and carbarsone,



One of the most important contributions to the chemotherapy of protozoal diseases has been the discovery of the effectiveness of quinquevalent antimony organic compounds in the treatment of visceral leishmaniasis. This type of infection causes much suffering and takes a great toll of life in India, Africa and South America. The death rate from such diseases has been greatly lowered in the past few years as a result of treatment with antimony compounds. At first antimonyl tartrates were used, but these proved to be much too toxic for use in the dosage required for satisfactory therapeutic results. The derivatives of phenylstibonic acid, prepared after a satisfactory synthesis had been worked out for the acid, proved superior to the antimonyl tartrates, tartar emetic type, in being less toxic for human and more toxic for the parasite. Important compounds of the quinquevalent type are stibamine, the sodium salt of para-aminophenylstibonic acid,



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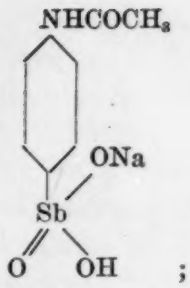
stibacetin or stibenyl,



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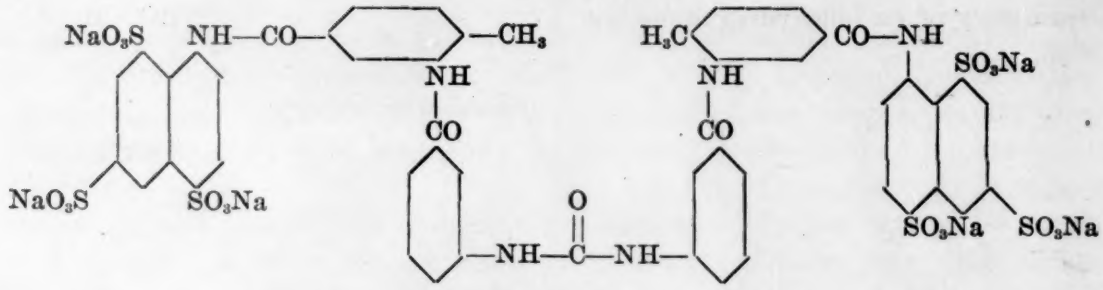
urea stibamine; neostam; the N-glucoside of stibamine; stibobsan, a stibacetin containing chlorine on the phenyl nucleus; and solustibosan, said to be a combination of hexonic acid with stibosan. Many other similar products have been prepared and tested. Claims are made for some of them which justify a thorough investigation of their clinical possibilities in both visceral and skin infections due to leishmania. The fact that these quinquevalent antimony compounds can be used in comparatively large doses without serious toxic results encourages one to believe that among the group will be found products that will effectively wipe out leishmaniasis, including the oriental sore.

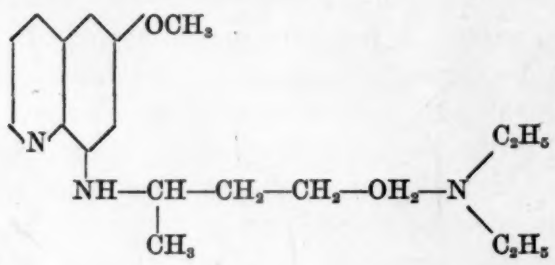
The success with organic arsenicals in the chemotherapy of syphilis has stimulated research to find better and safer drugs for the treatment of this and other diseases caused by similar agents of infection. In the last two decades scores of new organic compounds containing arsenic or bismuth have been made and tested. A few have proved useful. In particular certain bismuth compounds have been shown to be valuable adjuvants to the arsphenamine type of arsenical in the treatment of syphilis. More than two hundred bismuth compounds have been made and studied. The effective bismuth drugs appear to be less toxic than the arsenicals, but they are not good enough therapeutic agents to replace them. Arsphenamine and related arsenicals are still of inestimable value in the treatment of syphilis. It is probable that the bismuth compounds will ultimately replace mercury compounds in the chemotherapy of this disease.

Parasitic organisms of the trypanosoma type cause many diseases which cause great suffering and take a high toll in human lives throughout the infested areas of the world. Sleeping-sickness and fevers of tropical countries have received much attention in recent years. Some of the ablest investigators in the world have enlisted in the army of scientists fighting these diseases and the results obtained in the chemotherapy of trypanosomiasis are promising. The most amazing result is the success in treating sleeping-sickness with complex urea derivatives containing no metal. Numerous arsenic and antimony organic compounds had been studied with discouraging results. Then, it was found that the complex compound,

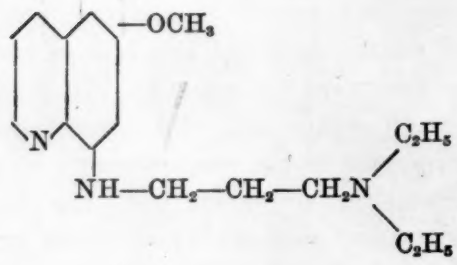


known under the international aliases of Germanin (Bayer 205), in Germany, Moranyl (Fourneau 309) in France and Antropol in Great Britain, was highly effective, particularly in the early stages of the disease before the central nervous system had been attacked. The remarkable thing is that the slightest deviation from the above structure results in a lowering of the trypanocidal activity. Why such a structure is essential no one knows. Many other organic compounds of widely different molecular architecture have been studied, but none of them has been particularly effective.

Of the several parasitic diseases studied intensively during the last decade none has received more attention than malaria. The chemotherapy of malaria has made definite progress. The most promising results have been obtained with quinoline and acridine derivatives. While none of these gives entire satisfaction, those of the type of plasmoquine,



rhodoquine,



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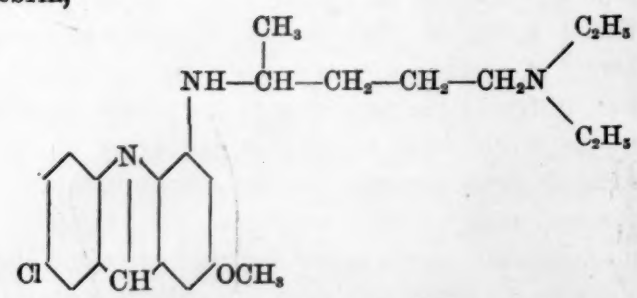
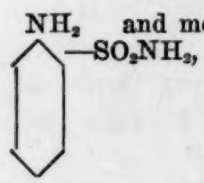
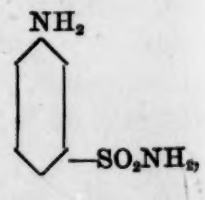


are certainly valuable adjuvants to quinine in the treatment of malaria. The ideal drug to combat the several phases of malarial infection is still to be discovered. The greatest obstacle to progress is the lack of knowledge of the mechanism of the drug action and what properties a compound should have to be effective. In spite of all the work done to date nothing definite can be said about the relation of chemical structure and parasiticidal action. It is possible that certain physical properties are essential and that the structural feature of the molecule is important only in making possible the required geometric arrangement for making these effective. Much more evidence from various sources must be secured and correlated before this problem is solved.

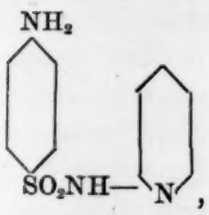
One of the most important, perhaps the most important contribution to the advancement of chemotherapy, is the recent discovery that p-aminobenzenesulfonamide (sulfanilamide) is an effective drug in combating certain diseases due to bacterial infections. With this begins a new era in medicine—the era of chemotherapy of bacterial diseases. This is the direct result of sustained research, in spite of discouraging results. With the exception of a few compounds that proved to be effective in the treatment of infections of the urinary system, no light had broken to dispel the darkness of the wilderness in which scientific investigators groped until the sulfanilamide star rose above the horizon. This shed its rays immediately over the entire world and illuminated the paths of research chemists through the realms of the unknown enabling them to bring forth hosts of sulfanilamide close relatives for study as chemotherapeutic agents. There is no complete record of all the sulfanilamides made but it is safe to estimate that they now exceed two thousand. Of this large number but few are valuable drugs. Why? In spite of all the accumulated evidence this question can not be answered yet.

Sulfanilamide,  , is effective in many infectious diseases, while its twin sisters orthanilamide,  and metanilamide, 

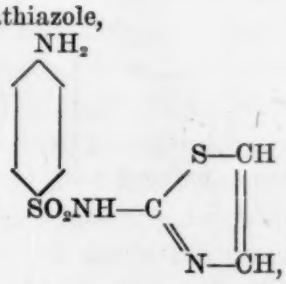
are inactive. This difference in behavior suggests that sulfanilamide must possess some significant property not shared by the other two members of the family. This must be responsible for its activity. Just how it acts and on what it acts are not definitely established. At present it is safe to say that the drug retards the growth of bacteria. Whether this is primarily due to changes brought about in the cycle of events involved in the reproduction of the cells or whether it concerns the food-assimilating functions of the bacteria can not be determined from the available evidence. It is evident that a thorough study of the metabolism and growth of bacteria with active and inactive sulfanilamides should throw some light on the important features of the mode of action of the drugs. The solution of this problem will serve to establish a fundamental basis for the further study of chemotherapy of infectious diseases.

The results obtained with sulfanilamide have been, in many cases, dramatic. In the short time it has been in use it has proved particularly effective in the treatment of infectious diseases, such as erysipelas, scarlet fever, tonsilitis, mastoiditis, meningitis (both streptococcal and meningococcal), peritonitis, puerperal fever, septicemia, osteomyelitis, streptococcal pneumonia and gonorrhea. Infections that proved fatal in practically all cases now clear up with its aid, and recovery follows. Many lives have been snatched from the jaws of death with it.

Of the sulfanilamide derivatives that have proved to be effective in experimental infections, sulfapyridine,



, and sulfathiazole,



appear at present to be particularly important. They are better than sulfanilamide against pneumococcal and staphylococcal infections. Sulfapyridine has been tested clinically and its value as a drug for the treatment of pneumonia established. In experimental pneumococcal infections sulfathiazole appears to be about as good as sulfapyridine, but not sufficient clinical data are yet available to show what place it will take in the chemotherapy of pneumonia. At present the evidence shows the product to be superior to both sulfanilamide and sulfapyridine in the treatment of staphylococcal infections. Further clinical evidence is needed to show its relative importance as a therapeutic agent.

The scope of chemotherapy is wide. Daily, new results appear showing that the sulfanilamides have helped in this and in that disease. There is some evidence that sulfanilamide and certain of its derivatives have a beneficial effect on the course of experimental tuberculosis in guinea pigs, but so far the clinical experiments have not demonstrated that they are valuable therapeutic agents for the treatment of tuberculosis in humans. There is also some evidence that certain of the sulfanilamides are effective for the treatment of gas gangrene, trachoma, undulant fever and lymphopathia venereum.

Enough has been said to indicate that real progress has been made in chemotherapy during the past few years. The results justify the hope that in the not too distant future a definite basis may be established for an understanding of the physical and chemical processes involved in health and disease. Then, the complexity of the human organism with its delicately adjusted mechanism will be better understood and appreciated. It will be seen that man is not necessarily "the animal of the wig, the ear-trumpet, the glass eye, the porcelain teeth, the wooden leg, the silver windpipe"—"a creature that is all mended from top to bottom"—"a basketful of pestilent corruption, provided for the support and entertainment of microbes"; but instead he is "a shop of rules, a well-trussed pack, whose every parcel underwrites a Law." He is a part of a great experiment. His life is like a string of many different colored beads whose beauty and usefulness depend upon the cord that binds them together in unity of pattern and purpose.

LO, THE POOR WHALE!

By Dr. ROBERT CUSHMAN MURPHY

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INFORMATION submitted to the International Whaling Conferences of the past three years discloses the long-expected decline of the fishery in its last and richest field, the Far South. The true measure of the decline lies not in the absolute number of whales killed, which may have been greater than ever before, but rather in the number taken per catching unit. On this basis the 1938–39 season is to be reckoned the

poorest in Antarctic history unless the season that ended in March, 1940, proves even worse. Detailed figures for neither period have yet been published.

Despite the publicity given to modern whaling, most Americans probably still think that the peak of slaughter on the high sea came at some time between the era of "Moby Dick" and the fading away of the Yankee fleet toward the close of the nineteenth century. In 1846, 736 American whaleships, and 230 craft of other nations, were cruising. New Bedford, the last stronghold, reached its top in 1857, when 329 vessels and 10,000 seamen called that city their home port.

It is possible that in the heyday of oldtime whaling as many as 12,000 great "fish," comprising sperm whales, right whales, bowheads and humpbacks, may have fallen within a single calendar year to all the hand harpoons and lances in action. The oil produced in 1846 by American crews from twenty-seven ports, according to Starbuck's tables of the year 1878,[1] totalled 302,918 barrels of thirty-one and one half gallons. Taking into account the average yield of the species forming the prey, this might indicate a kill of approximately 7,500 whales by ships under our flag alone.

All such older records pale into insignificance when compared with those for the recent world catch, as issued annually or more often by the Committee for International Whaling Statistics. Between 1920 and 1940 approximately half as many whales were killed as during the whole preceding history of whaling. The total for three centuries (1620–1920) is believed to have been not more than a million, or an average of about 3,000 whales a year. Subsequently the average has been well above 25,000 a year.[2] The columns for 1937–38 show a slaughter of 54,664 whales, the largest number ever killed; 46,039 of these were taken in Antarctic waters within a summer period extending from October or November at least into April, the remaining 8,625 during part or all of a twelve-month season in the Arctic, the North Pacific, the North Atlantic, along the African coast and off the shores of South America and Australia.[3] The number of whales killed in all waters between 1919 and 1938, inclusive, reaches the staggering total of 543,622. Details of oil production, in barrels of the modern fifty-gallon capacity, are available for a still longer period; between 1909 and 1938 it summed up to 40,257,700 barrels.

[1] U. S. Commission of Fish and Fisheries, part IV, Report of the Commissioner for 1875–1876, Appendix A, pp. 434–442, Washington, 1878.

[2] *Cf.* "Whales." Hearing before a special committee on wild life resources, United States Senate, 72d Congress, 1st Session, Washington, 1931; testimony of A. B. Howell, p. 2, and of Remington Kellogg, p. 21.

[3] "International Whaling Statistics," edited by the Committee for Whaling Statistics appointed by the Norwegian Government, XIII, Oslo, 1939; also parts I–XII, Oslo, 1930–1939.

Such figures verge on the astronomical—or the numerical ideas associated with the current price of public administration! The stupendous quantities of flesh and blood now being taken from the sea by whaling operations can be grasped, perhaps, only by reference to the size of an individual whale. Eighty-two feet is about the average length of all the blue whales caught during the decade ending in 1938. A carcass of the sort might weigh eighty tons, the equivalent of twenty male African elephants or of more than a thousand men. The human species, it must be remembered, represents in the world of to-day neither a small nor an average-sized animal, but a relatively huge one. There are, indeed, only a few hundred kinds of creatures of greater bulk than man himself, these comprising numerous other mammals, certain fishes and reptiles, a handful of flightless ostrich-like birds and a few invertebrates such as giant squids. But about a million and a half described species are so much smaller than man, in varying degree, that an average drawn from one full-grown example of each of the known kinds, whales included, would give us a product not very different in size from a housefly.

The vital statistics tabulated in several hundred pages of the Norwegian reports referred to above were not compiled with the object of satisfying idle curiosity. Their inception lay in a deep-seated concern for waning resources needed by all nations and indispensable for the well-being of several. The original recommendation came from the International Council for the Study of the Sea, at a meeting held at London on April 10, 1929, which led in turn to the organizing of a central bureau by the Norwegian Government and to the first publication, in 1930, of tables covering the preceding ten-year period. Subsequently the committee still further extended the record by compiling, from all sources, figures relating to modern steam-whaling from its beginning off the northern coast of Norway in 1868. The first thirty-five years of such whaling proved relatively picayune, the largest annual number of victims during the nineteenth century being 1,993 whales, taken in 1898. It was not until 1904, with the entry of steam-catchers into the Atlantic section of the Antarctic, that the kill began to mount into impressive figures.

As a business proposition modern whaling has had its vagaries, a local falling off in the returns becoming apparent as soon as the size and perfection of equipment proved too formidable for the stock of whales to bear. The Newfoundland whale fishery, for example, began from shore stations in 1898, reached its peak in 1904 (1,276 whales), and fell away to five catching-craft and a negligible return in 1913. Whaling from the Norwegian coast and from many other northern-hemisphere stations has had a similar history, but the opening of the Antarctic grounds lent

enormous new impetus to the exploitation of wealth hich, fallaciously, seemed "inexhaustible."

The first sign of unmistakable danger showed itself a shift in the species of whales that made up the eponderant part of the catch at South Georgia, 1,200 iles east of Cape Horn. Originally more than 95 er cent. of the whales there captured were humpacks, but as these became rapidly decimated the end was progressively toward the finback and blue hales, which have lately been the mainstay of the shery. The blue whale, with a length sometimes exeeding 100 feet, is the largest creature that lives in he world to-day or that ever has lived. In the averge summations of whalemen, with reference to derivation of oil, fertilizer and other products, one blue hale is taken to equal two finbacks, two and a half umpbacks or six sei-whales.

The first restriction in pelagic whaling came in 1932, purely as a result of economic necessity. The whale il market was glutted and Norway's great fleet remained in port. Only Japanese shore-whaling has shown a rather consistent balance, related to supply and demand at home rather than to the uncertainties of a world market. This is because the whales taken in Japan have always been used primarily as human food, for which reason each carcass can be made to yield a far higher monetary return than that based principally upon the sale of oil. Between 1910 and 1932 Japanese domestic whale-catchers have at no time been fewer than twenty nor more than thirty-five. Throughout this period the average number of whales taken annually by each boat has been fifty-five, or roughly one a week, as against a corresponding annual average of 188 for waters around South Georgia. These Japanese data, however, refer only to vessels working offshore from home ports. Between November 1, 1937, and March 26, 1938, as well as during the two subsequent southern-summer seasons, Japan has carried on whaling in the Antarctic Ocean, with at least four floating factories and thirty catchers, entirely unimpeded by the limitations that other whaling nations have finally imposed upon themselves.

The first voluntary attempts to reduce the number of whales killed were influenced by the world financial crisis and realized by agreement between commercial companies. In this move labor had an equal share with capital, even to the point of threatening a general strike. The whale quota, that is the absolute number of animals in "blue whale equivalents" which each company was entitled to shoot, was mutually determined, in addition to which special efforts were made to assure the utmost possible recovery from each carcass. Cow whales seen to be accompanied by calves were granted immunity at all seasons. With very few exceptions, such regulations seem to have been scrupulously honored. Under the stimulus of action by the Norwegian Parliament in 1934, all Norwegian companies and all but two of the foreign whaling companies then operating in the Antarctic further accepted seasonal restrictions in waters south of latitude 50° S., and showed evidence of enlightened self-interest, if not of humanitarianism, by endeavoring to cooperate heartily with purely scientific investigations into the life history of whales, such as those sponsored by the British Discovery Committee. Gradually all whaling concerns have entered the concordat, with the exception of the Japanese.

Notwithstanding these commendable attempts to repair a situation so palpably intolerable that it could end only in disaster, successive reports of the Committee on International Whaling Statistics during the 1930's developed a monotonous tone in reporting that the previous season's catch had again been "the largest ever recorded." In 1936 the governments of Great Britain and Norway pledged themselves to curtail the season everywhere south of 40° S. latitude to the short period between December 8 and March 7, and still further to cut down the number of whale-catchers entitled to accompany each floating factory. During the following season, however, two Japanese expeditions and one German conducted their carnage without restrictions of any sort.

Ultimately, in June, 1937, the situation attained full-fledged international status as regards the richest and ultimate field, namely, all the free waters and national territories lying beyond latitude 40° S. Stringent regulations for this great area, even to "game laws" covering a minimum legal size for whales of each species, were officially approved by the South African Union, Argentina, Australia, Germany, Great Britain, Ireland, Northern Ireland, New Zealand and the United States; only Japan, among the effective nations, still proved recalcitrant.

German pelagic whaling has, of course, been interrupted by the war. Whether it can ever be resumed is at least questionable because many of the leading Norwegian operators are now convinced that the whole exploitation is certain to fall below its practicable economic threshold within the next five years. German whaling aims are concerned largely with food-fats, specifically whale-oil margarine, which are also of prime importance in the Scandinavian countries and elsewhere. American consumption of the oil, on the other hand, has thus far related chiefly to the manufacture of soap. The ambitious nature of the German program is set forth in the best compendium yet published.[3] This deals with Antarctic colonization and the oceanic environment, the history of

[3] Nicolaus Peters, editor. "Der neue deutsche Walfang." 237 pp. Hamburg, 1938.

whaling, problems of international regulation, the newly built German fleet, catching and reducing methods and equipment, the biology of whales and the nature and chemistry of both raw materials and derivatives. The book is fully illustrated and closes with a well selected bibliography of 182 titles and an index. Particularly informing are the tables listing, as of 1938, the mother-ships, oil and guano reduction plants and 432 whale-catching vessels of 61 commercial companies representing ten nations, the British Empire being treated as a unit.

In 1938–39, twenty-eight floating factories, with individual registered tonnages up to 21,846, and 281 whale-catchers were at work in Antarctic waters. In 1939–40, the average number of catchers per mother-ship is stated to have been still higher, though precise figures are not yet available. The Japanese ships carried larger crews than similar vessels under other flags, but Japanese oil recovery per whale was the lowest in the field. Somewhat more than 11,000 men are now engaged in Antarctic whaling; the oil from Antarctic waters totaled during the latest season of record (1937–38) more than half a million tons, which fetched an average price of $65.00 a ton, or only 50 per cent. of the *lowest* mean annual value for an earlier thirty-year term (1900–1929). The number of whales being slain is at least fourfold what the oceans can endure on a long-term basis, yet the goal of reasonable, and hence perpetual, utilization seems farther off than ever.

OBITUARY

FRIEDRICH EMICH

1860–1940

FRIEDRICH EMICH, professor emeritus of chemistry at the Polytechnic Institute of Graz, Austria, the originator of modern microchemistry, died at his home in Graz on January 22, 1940. He was born there on September 5, 1860, and received his primary and preparatory schooling in Laibach (at present Yugoslavia). He then attended the Polytechnic Institute in Graz from 1879 to 1884, majoring in chemistry. Four years later he was admitted to the faculty of the same institute as "privatdozent," becoming associate professor of chemistry the following year. In 1894 he was appointed to full professorship, a position which he held until his retirement in 1931. He was repeatedly elected dean and chancellor of the institute.

In recognition of his scientific achievements he was awarded several honorary doctor's degrees and was decorated by both the Imperial and the Republican Governments of Austria. In 1918 he was appointed corresponding member of the Austrian Academy of Science and became full member of that organization in 1928.

From 1882 to 1890 his scientific papers were chiefly in the field of organic chemistry, while from about 1890 to 1905 a series of papers in organic and general chemistry were published. The first microchemical paper appeared in 1893, dealing with a qualitative test for sulfur. His systematic investigations in microchemistry began not until seven years later and culminated in 1911 in the publication of the still standard microchemical text, "Lehrbuch der Mikrochemie." His most important contributions in the field of microchemistry included a comprehensive treatise on microbalances (1915), the development of methods of capillary technique (1915–1920), quantitative inorganic analysis (1920–1926), application of Schlieren phenomena to chemical reaction studies (1926–1931) leading to his final contribution in 1936, "Observation of Changes at the Critical Temperature of Certain Gases by Means of the 'Schlieren-Microscope.'"

In the field of organic microchemistry, that branch of microchemistry which overshadows in importance all others and which was universally recognized with the reward of the Nobel prize in chemistry to the late Professor F. Pregl, also of Graz, Professor F. Emich made the first and pioneering contributions, such as the micro Carius and Kjehldahl determinations. These initial successes of F. Emich formed the foundation upon which later the entire field of quantitative organic microanalysis was built by his colleague, F. Pregl. Thus the work of these two eminent Austrian scientists, the cautious and eminently refined technique of F. Emich and the sure and successful practical application of F. Pregl, eventually blended into one of the outstanding scientific monuments of former Austria.

Their contributions revolutionized organic chemical research, inasmuch as modern investigations in the field of hormones and vitamins could not possibly have been brought to the present heights without the combined work of these two investigators, whose lives were in many respects so similar. Their work was also not without due influence in the United States. Pregl's methods were introduced here in 1925 and Emich's in 1929. The American Chemical Society soon recognized the importance of this new branch of chemistry by establishing the Division of Microchemistry.

Professor F. Emich, who is survived by his wife and two daughters, was the ideal of a pure scientist. Possessed of an extremely pleasing but nevertheless commanding personality, he combined thorough scientific knowledge with supreme refinement of experimental technique and infinite patience. Being a superb

lecturer, he would go to extreme pains in experimental preparation for his famous microchemical demonstrations, which never failed and of which the writer was repeatedly a fortunate witness. Thus the remarks made in the lecture in which Professor Emich demonstrated "the breathing of a rose petal" by means of the Schlierenprojectoscope, ". . . and now just imagine if we would wear glasses of similar optical design, a new world would open to us, a world unexcelled in phantastic aspects . . . ," revealed the qualities of an eminent scientist who also possessed the rare gift of being able to blend esthetics with science to a harmonious symphony.

JOSEPH B. NIEDERL

WASHINGTON SQUARE COLLEGE,
NEW YORK UNIVERSITY

RECENT DEATHS AND MEMORIALS

DR. DAVID M. MOTTIER, emeritus professor of botany at Indiana University, died on March 24 at the age of seventy-five years.

DR. CHARLES L. REESE, formerly head of the department of chemistry and a member of the board of directors of E. I. du Pont de Nemours and Company, died on April 12 at the age of seventy-seven years.

DR. GLENN E. CULLEN, professor of pediatrics at the College of Medicine of the University of Cincinnati and director of the laboratories of the Children's Hospital Research Foundation, died on April 10 at the age of fifty years.

THE *Journal* of the American Medical Association reports the formation of an organization to raise an endowment fund of $150,000 to establish fellowships in neurology as a memorial to the late Dr. Frederick Tilney, formerly professor of neurology and neuroanatomy at Columbia University. According to the plans, the principal of the memorial fund will be in the custody of the trustees of Columbia University.

A GRINNELL NATURALISTS SOCIETY of the University of California at Berkeley has been organized to commemorate the work of the late Professor Joseph Grinnell, who was for thirty-one years the director of the museum of vertebrate zoology of the university.

SCIENTIFIC EVENTS

PUBLICATION OF A NEW PHYSIOLOGICAL JOURNAL IN SCANDINAVIA

THE following announcement dated March, 1940, has been received from Professor August Krogh, of Copenhagen, by Dr. A. J. Carlson, of the University of Chicago.

Last year we had some talk about the future of *Skand. Arch.* We have now tried to obtain an arrangement to take over the Journal (from the publishers), but failed, and it has been decided to discontinue the "Archiv" and start a new journal on a strictly Scandinavian basis with Liljestrand as editor-in-chief and with assistant editors in the single countries to secure a high standard for the papers accepted. The journal is to be called *Acta Physiologica Scandinavica*, and we expect to send out the first number before long to a large number of physiologists, pharmacologists, biochemists and libraries. The *Acta* will be open to papers from Scandinavian authors and people working in Scandinavian laboratories, and I trust that the number of papers in English will show a marked increase, the more so as we must face the probability that it will be officially or inofficially excluded from Germany. We shall be very grateful if you will draw the attention of our colleagues in the United States and Canada to our new venture and help us secure a sufficient number of subscribers.

We are well aware of the difficulties. Our countries are being impoverished by the war at an appalling rate and are under a constant menace, but we are determined (even our colleagues in Finland) to carry on the scientific work and to do our best to make this new venture a success.

AWARD OF GUGGENHEIM FELLOWSHIPS

SEVENTY-THREE fellowships with stipends amounting to $165,000 to assist research and creative work have been announced by the John Simon Guggenheim Memorial Foundation. The foundation, established in 1925 by former United States Senator and Mrs. Simon Guggenheim as a memorial to a son to assist original work by scholars and artists, in the past fifteen years has granted 913 fellowships and $2,082,000 to assist its fellows to carry on their work.

This year, on account of the wars in Europe and the Far East all fellows, except one whose plans will take him to the Near East, will work in the Western Hemisphere. Twelve will go to Latin America, and the rest will work in the United States and in Canada. Among those who will work in the United States are six Canadians appointed under a recent extension of the fellowships to Canada. The annual Guggenheim fellowships for Latin American scholars and artists, another part of the foundation's plans for granting fellowships in this hemisphere, will be awarded in June.

The Guggenheim fellowships are granted to scholars and artists who by their previous work have shown themselves to be persons of unusual ability. Men and women, married and unmarried, of all races and creeds, who are citizens or permanent residents of the United States, citizens of Canada and of certain Latin American countries, are eligible on equal terms. The fellows

are usually of ages between 25 and 40 years. This year their average age is thirty-seven years. The stipends are usually $2,500 a year.

Of the fellows chosen this year thirty-seven are free-lance scholars and artists. Twenty are not college trained. Five are women. They are residents of twenty-two states and of two Canadian provinces. McGill University leads with three members of its faculty. Clark University and the Universities of California, Michigan and Pennsylvania have two each. Twenty-five colleges, universities and research institutions have one fellow each drawn from their staffs. Two of the fellows are Negroes.

The seventy-three fellows were selected from among more than 1,700 applicants. Fellowships awarded in the sciences are:

DR. ALFRED MÉTRAUX, ethnologist, who, on his renewed fellowship, will write a book to be entitled "The Ethnology of the Gran Chaco." Dr. Métraux spent his first Guggenheim Fellowship in that area studying the culture of the primitive Indians there.

DR. ALFRED IRVING HALLOWELL, professor of anthropology in the University of Pennsylvania, will write a book on personality in primitive communities, based upon the results of his observations of an aboriginal hunting people.

DR. LUTHER SHEELEIGH CRESSMAN, professor of anthropology and director of the Museum of Natural History, University of Oregon, will study the relation of the prehistoric south-central Oregon cultures to those of the Southwest.

DR. ISABEL T. KELLY, a research associate of the University of California, who will make ethnographic and archeologic investigations in southwestern Mexico.

DR. GEORGE KATONA, research psychologist, New York City, will make studies in the field of the psychology of learning with special reference to the differences in learning by understanding and learning by memorization and drill.

DR. JESSE DOUGLAS, Brooklyn mathematician, for research in mathematical analysis and geometry with some applications to mathematical physics. Dr. Douglas was awarded the Fields Medal by the International Congress of Mathematicians meeting in Oslo, in 1936.

DR. RAYMOND L. WILDER, professor of mathematics in the University of Michigan, for researches in the field of topology, particularly in the theory of local connected spaces and of generalized manifolds.

DR. AUREL FRIEDRICH WINTNER, associate professor of mathematics in the Johns Hopkins University, for the preparation of a monograph, in collaboration with Dr. Norbert Wiener, a former fellow, in the field of mathematical theory of probability and statistics.

DR. GORDON PALL, assistant professor of mathematics in McGill University, who will write a book on the arithmetical properties of quadratic forms.

DR. HAROLD ERNEST VOKES, assistant curator of invertebrate paleontology in the American Museum of Natural History, New York City, will make a study, in cooperation with the American University at Beirut, Syria, of the stratigraphy and invertebrate paleontology of the Lebanon Mountains.

DR. RAYMOND E. CRIST, instructor in geography at the University of Illinois, will write a book on the human geography of the Venezuelan Andes.

DR. CHESTER STOCK, professor of paleontology at the California Institute of Technology, Pasadena, who will continue his vertebrate paleontological reconnaissance of Mexico, begun last year on his first Guggenheim fellowship.

DR. RAYMUND L. ZWEMER, assistant professor of anatomy at the Medical School of Columbia University, will work in South America with Dr. B. A. Houssay, professor of physiology in the University of Buenos Aires. Dr. Zwemer's project is a scientific study of the factors involved in the maintenance, by living cells, of a differential permeability to electrolytes.

DR. BERRY CAMPBELL, assistant professor of anatomy at the Medical School of the University of Oklahoma, who will make an investigation of the integrative mechanisms of the spinal cord with particular reference to the basic locomotor behavior patterns.

DR. GEORGE THOMAS JOHNSON, research assistant and lecturer in botany, Washington University, St. Louis, who will make a biologic and taxonomic study of the lichens of tropical America.

DR. HENRY K. SVENSON, curator of the Brooklyn Botanic Garden, who will investigate the relationship of the flora of western South America to that of the Galapagos Islands. Dr. Svenson has already worked in the Galapagos, and his fellowship will be used for plant exploration in the opposite mainland of South America.

DR. STANLEY ADAIR CAIN, associate professor of botany, University of Tennessee, for the preparation of a book on the concepts and methods of geobotany.

DR. KATHERINE ESAU, assistant professor of botany and assistant botanist at the College of Agriculture, University of California, for studies of the anatomy and physiology of vascular plants.

DR. FRANKLIN P. METCALF, professor of botany, Lingnan University, Canton, China, for the preparation of a monograph on the flora of the Province of Fukien, China. Dr. Metcalf will work at the Arnold Arboretum of Harvard University.

DR. GREGORY PINCUS, visiting professor of experimental zoology at Clark University, who will, on his renewed fellowship, continue his investigations of the developmental physiology of mammalian eggs and embryos.

DR. MYRON GORDON, research zoologist of New York City, who will continue his genetic studies of species and varieties found in nature and his studies of neoplastic diseases in vertebrate animals.

DR. DAVID LION DRABKIN, assistant professor of physiological chemistry at the Medical School of the University of Pennsylvania, who will carry on researches in the field of biological oxidation-reduction processes with Professor W. Mansfield Clark at the Johns Hopkins University.

DR. JOHN TILESTON EDSALL, associate professor of bio-

logical chemistry in the Harvard Medical School, for studies of the physical chemistry of amino acids, peptides, proteins and related compounds.

Dr. David Dennison, professor of physics, University of Michigan, for researches into molecular structure.

Dr. Aristid V. Grosse, chemist of Bronxville, N. Y., for investigations of catalytic reactions of organic compounds and investigations of the products of neutron bombardment of uranium, protactinium and thorium, at Columbia University.

Dr. Arthur C. Cope, associate professor of chemistry, Bryn Mawr College, for studies of the phenomenon of tautomerism.

THE FINNEY-HOWELL RESEARCH FOUNDATION, INC.

The Finney-Howell Research Foundation, Inc., of Baltimore, Md., announces that, at the annual meeting held in March, 1940, fellowships for research into the cause or causes and the treatment of cancer were renewed for the following:

Paul Clarence Aebersold, working at the Radiation Laboratory of the University of California at Berkeley.

Geoffrey Malcolm Badger, working at the Royal Cancer Hospital (Free) at London, England.

Lloyd William Law, working at the Roscoe B. Jackson Memorial Laboratory at Bar Harbor, Maine.

Joseph Lewis Melnick, working at Yale University School of Medicine at New Haven, Conn.

John Frederick Menke, working at Stanford University Hospital, at San Francisco, California.

John Lewis Wood, working in the Division of Chemistry, Harvard University, at Cambridge, Mass.

Paul C. Zamecnik, working at the University of Carlsberg, at Copenhagen, Denmark.

New fellowships were awarded as follows:

Julius Charles Abels, working at the Memorial Hospital for Cancer at New York City.

Mark A. Graubard, working at Clark University, Worcester, Mass.

John Wade Howard, working at Thorndike Memorial Laboratory, Boston City Hospital.

Bernerd E. Kline, working at the Department of Physiology, University of Wisconsin.

Margaret Nast Lewis, working at Crocker Radiation Laboratory, the University of California at Berkeley.

Alfred Marshak, working at the Radiation Laboratory, the University of California at Berkeley.

Dr. George O. Gey was also awarded a grant of $2,000 to carry on his work in cancer at the Johns Hopkins Medical School.

January 1, 1941, has been fixed upon as the closing date for filing application for 1941 awards.

THE INDUSTRIAL RESEARCH INSTITUTE

The Industrial Research Institute, New York City, will hold its second annual meeting at the laboratories of the Procter and Gamble Company and at the Queen City Club, Cincinnati, on April 26 and 27. Maurice Holland is executive officer of the institute. Newly elected officers for the current year will be installed at the meeting. Present relations between industries and universities on research and how such relations may be made more effective will be the main topic of discussion. Dean Edward L. Moreland, professor of electrical engineering and head of the department of the Massachusetts Institute of Technology, and Dean Charles Ellison McQuigg, of the College of Engineering of the Ohio State University, will lead the discussions from the university point of view. Two industrial executives whose names will be announced later will discuss the subject from the standpoint of industry. Other subjects on the agenda are "Selection of College Graduates" and "Project Selection and Evaluation," to be led, respectively, by Dr. R. S. Uhrbrock, of the Industrial Relations Division of the Procter and Gamble Company, and by W. N. Tuttle, research director of the General Radio Company, Cambridge, Mass. There will be a tour through the Procter and Gamble Research Laboratories and plant at Ivorydale. Delegates will also visit the plant and laboratories of the Champion Paper and Fiber Corporation at Hamilton, Ohio, following the adjournment of the meeting.

The Industrial Research Institute, which is affiliated with the National Research Council, was organized to promote, through the cooperation of its members, constant improvement of methods and more efficient and better management in industrial research. The institute comprises representatives of industrial concerns who are leaders in their respective fields of research.

THE BICENTENNIAL WEEK CELEBRATION OF THE UNIVERSITY OF PENNSYLVANIA

The program of the Bicentennial Celebration Week of the University of Pennsylvania will open on Sunday, September 15, and will continue through Saturday, September 21. It will include the following events:

General sessions, symposia and conferences, to which many of the world's most eminent scholars will contribute.

Cultural and scientific exhibits illustrative of the progress of civilization through the ages.

Laboratory and clinical demonstrations of new techniques employed in engineering, chemistry, medicine, physics and other fields.

Convocation for the conferring of honorary degrees.

Addresses by prominent alumni and undergraduates of Pennsylvania. Presentation of Bicentennial Fund.

Parade of graduates. Class reunions. Tours of the campus. Special events for undergraduates.

Concerts by University Band and the Glee Club. Receptions, dinners and luncheons. Water carnival and fireworks display.

After religious services on Sunday, there will be a series of scholarly addresses appropriate to a program which is designed not only to constitute a tribute to

the University of Pennsylvania, but to focus attention upon the contributions which higher education everywhere has made, and can continue to make, to the betterment of mankind. These addresses will be delivered at general sessions, which will precede symposia and group conferences in the humanities, natural sciences, social sciences, medical sciences and religion. Each speaker has been selected because of the outstanding position he occupies in his particular field.

Those coming from England to address the general sessions include Sir Thomas Lewis and Sir Henry Dale in medicine; Sir William H. Beveridge, economist, master of University College, Oxford; Dr. Alan J. B. Wace, professor of classical archeology at the University of Cambridge; from France, Professor Etienne Gilson, historian; Dr. Charles Cestre, professor of American literature and civilization, University of Paris, and Dr. Jacques Maritain, professor of philosophy at the Catholic Institute, Paris; from Denmark, Dr. Thorvald Madsen, of the State Serum Institute at Copenhagen; from Germany Dr. Werner C. Heisenberg, professor of physics at the University of Leipzig; from Switzerland, Dr. William E. Rappard, political science.

Addresses at the general sessions will be given by Hu Shih, Chinese ambassador to the United States; Dr. Frank B. Jewett, president of the Bell Telephone Laboratories; Dr. Evarts A. Graham, surgeon and member of the faculty at Washington University, St. Louis; Dr. Hans Zinsser, professor of bacteriology and immunology at the Harvard Medical School; Dr. Lawrence J. Henderson, biological chemist, Harvard University, and Dr. Herbert Spencer Jennings, emeritus professor of zoology at the Johns Hopkins University.

At the forty symposia and conferences which will follow the general sessions the program will provide, as a rule, for a keynote address, as well as one or two shorter addresses and an open discussion.

SCIENTIFIC NOTES AND NEWS

DR. ERNEST O. LAWRENCE, professor of physics and director of the Radiation Laboratory of the University of California at Berkeley, will give an illustrated lecture entitled "Bombarding Atoms" on the evening of Monday, April 22, before the annual meeting in Washington of the National Academy of Sciences.

PROFESSOR C. E. MCCLUNG, director of the Laboratory of Zoology of the University of Pennsylvania, reached the age of seventy years on April 5. A surprise party was held for him at the home of his daughter, Ruth McClung Jones. A correspondent writes: "After a dinner attended by Dr. and Mrs. McClung and a few intimate friends, members of the staff of the department of zoology and their wives arrived in time to share in the ice cream, coffee and birthday cake. The guests brought a varied assortment of 'presents.' These included grasshoppers made out of various materials (one realistic one was constructed of parsnips), models of chromosomes, picture books, toy microscopes and other toys such as globes, ships and a mechanical snake. Each 'present' was accompanied by a rhyme or jingle, all of which provided much hilarity for this jolly occasion. In addition Dr. McClung received many telegrams and letters of felicitation."

THE prize ($1,000) in pure chemistry of the American Chemical Society, provided this year by Alpha Chi Sigma, has been awarded to Dr. Lawrence Olin Brockway, assistant professor of chemistry at the University of Michigan, for his work on the determination of molecular structure by electron diffraction methods. The Francis P. Garvan Gold Medal to honor an American woman for distinguished service in chemistry has been awarded to Dr. Mary E. Pennington, of New York City, an authority on the refrigeration of perishable foods. Presentation of the awards will be made at the meeting of the society to be held in Detroit from September 9 to 13.

OLE SINGSTAD, chief engineer of the New York City Tunnel Authority and a member of the Royal Norwegian Academy of Sciences, received the rank of Knight First Class of the Order of St. Olav at the command of King Haakon VII of Norway at ceremonies held on April 8 in the offices of the Tunnel Authority. The presentation was made by Wilhelm Munthe Morgenstierne, Norwegian Minister to the United States, and Rolph A. Christiensen, Norwegian Consul General of New York City. The decoration was given in recognition of "distinguished accomplishments in the engineering field and contributions to Norwegian interests in New York." Mr. Singstad was engineer of design for the Holland Tunnel and devised the transverse system of tunnel ventilation that has been adopted by tunnel authorities throughout the world.

DR. WILLIAM C. ANDERSON, dean emeritus of the Brooklyn College of Pharmacy, was the guest of honor on April 10 at a dinner given in celebration of the seventy-fifth birthday, closing the annual convention of the New York Pharmaceutical Council.

THE Cameron Prize of the University of Edinburgh has been awarded to Professor E. C. Dodds, Courtauld professor of biochemistry in the University of London, for his work on synthetic oestrogens.

ACCORDING to a Reuter's dispatch to the London *Times*, Sir Harold Carpenter, professor of metallurgy in the Royal School of Mines, London, has been chosen by the Metallurgical Society of Japan as winner of the Honda Prize. He is the first foreigner to receive the award—a gold cup and £300.

THE Goethe Medal of Science and Art of the German Empire has been awarded to Dr. Ludwig Prandtl, professor of applied mechanics at the University of Göttingen.

The British Medical Journal states that at the annual meeting of the Royal Asiatic Society of Bengal on February 5 the award of the Barclay Memorial Medal for 1939 was made to Major-General Sir Robert McCarrison, "for conspicuously meritorious contributions to medical science, with special reference to India." The *Journal* also reports that at a recent meeting of the Academy of Sciences of Ferrara a medal known as the *Nummus aureus* was conferred on the following leaders of Italian medicine: the surgeon and Senator Raffaele Bastianelli; Dr. Francesco Delitala, professor of clinical orthopedics; Senator Davide Giordano, of Venice, author of several surgical works; General Loreto Mazzetti, director of military hygiene; Senator Alberto Pepere, professor of morbid anatomy, and Vittorio Putti, professor of clinical orthopedics at Bologna.

DR. EDWARD LEE THORNDIKE, professor of educational psychology and director of the Division of Psychology of the Institute of Educational Research at Teachers College, Columbia University, will retire from active service on July 1.

DR. KARL E. MASON, associate professor of anatomy at Vanderbilt University, has been appointed head of the department of anatomy of the School of Medicine and Dentistry of the University of Rochester. He succeeds Dr. George W. Corner, who, after serving since 1924, resigned last autumn to become director of the department of embryology of the Carnegie Institution. Dr. Robert K. Burns, Jr., associate professor of anatomy at Rochester since 1928, will go with Dr. Corner to Baltimore.

IVAN CHARLES CRAWFORD, professor of civil engineering and dean of the School of Engineering and Architecture of the University of Kansas, has been appointed dean of the College of Engineering of the University of Michigan; Dr. Charles Fremont McKhann, assistant professor of pediatrics and communicable diseases at the Harvard Medical School, has been appointed associate professor of pediatrics and communicable diseases.

PROFESSOR WILLIAM ALLAN has been elected chairman of the department of civil engineering in the School of Technology of the College of the City of New York. He succeeds Professor Frederick Skene, who retired last month after serving eighteen years as head of the department.

THE council of the University of Manchester has appointed Dr. C. W. Wardlaw, officer-in-charge of the Low Temperature Research Station, Trinidad, to the Barker chair of cryptogamic botany in succession to Professor W. H. Lang, whose appointment terminates at the end of the present session.

THE Porter Fellowship of the American Physiological Society has been awarded for 1940–41 to Dr. Gordon K. Moe, of the department of physiology of the University of Minnesota, for studies with Professor C. J. Wiggers, of Western Reserve University.

PRESIDENT ROOSEVELT has appointed Charles E. Jackson, acting commissioner of the Bureau of Fisheries, as one of the representatives of the United States on the International Fisheries Commission established between the United States and Canada, to fill the position left vacant by the resignation of Frank T. Bell, formerly Commissioner, Bureau of Fisheries. The other representative of the United States is Edward W. Allen, of Seattle, Wash., who became secretary of the commission on December 14.

THE Smithsonian-Firestone expedition to West Africa, headed by Dr. William M. Mann, director of the National Zoological Park of the Smithsonian Institution, has arrived in Liberia and is making preparations for getting as large and representative a collection as possible of the mammals, birds and reptiles of that country. The expedition, which is a joint undertaking of the Smithsonian Institution and the Firestone Tire and Rubber Company, which maintains extensive plantations in Liberia, will obtain animals for the park in Washington.

J. C. MILLER, geologist in the Conservation Branch of the U. S. Geological Survey, left Washington on April 3 to undertake geologic investigations in and adjacent to the Konawa, Traugh and Tyrola oil fields in Seminole County, Oklahoma. D. F. Hewett recently returned to Washington from field conferences with Geological Survey parties engaged in the study of tin deposits in North and South Carolina, mica deposits near Spruce Pine, North Carolina, and manganese deposits in Campbell County, Virginia. These districts are among the numerous areas in the United States that are being studied by the survey in the program of review of domestic sources of strategic minerals and metals.

DR. LEO LOEB, professor of comparative pathology, emeritus, at Washington University, St. Louis, will give an address on April 22 at the National Cancer Institute of the U. S. Public Health Service on "The Significance of Hormones in the Origin of Cancer."

DR. A. C. IVY gave on the evening of April 19 the seventh annual Arno B. Luckhardt Lecture of the Delta Chapter of Phi Beta Pi of the University of Chicago Medical Schools. He spoke on "The Gastro-Intestinal Hormones."

PROFESSOR MARSTON T. BOGERT, of Columbia University, on March 16 spoke before the Rensselaer Polytechnic Institute Chapter of Sigma Xi. His subject was "The Chemist in a Chaotic World."

DR. WILLIAM G. MACCALLUM, Baxley professor of pathology at the School of Medicine of the Johns Hopkins University, delivered the annual Kober Lecture at the Georgetown University Medical School, Washington, on March 28. He spoke on the "Pathology of the Parathyroid Glands." The lecture commemorates the late Dr. George M. Kober, of Washington, and is given on his birthday. Dr. MacCallum was presented with the certificate and honorarium of $500 provided by the Kober Foundation.

BECAUSE of the uncertainties of transportation due to international affairs, the eighth series of Salmon Memorial Lectures, which were to have been given by the Russian psychiatrist, Dr. Alexander Luria, have been postponed. Dr. Nolan D. C. Lewis, director of the New York State Psychiatric Institute, who has been appointed in the place of Dr. Luria, will advance the date of his series of lectures to November, 1940. He will deliver a series of three lectures at The New York Academy of Medicine on November 8, 15 and 22. Salmon lecturers are selected each year on the basis of their scientific achievement, with particular reference to constructive contributions in the fields of psychiatry and neurology.

PROFESSOR DOUGLAS JOHNSON, of Columbia University, serving as one of the lecturers in the annual series on "Science in Progress," sponsored by the National Society of the Sigma Xi and discussing investigations of "The Mysterious Craters of the Carolina Coast" as illustrations of methods in scientific research, addressed Sigma Xi chapters and clubs during the period March 13–April 3 at the following institutions: Swarthmore College, the University of Maine, Denison University, the University of Illinois, Indiana University, the Rice Institute, the State University of Louisiana, the University of Kansas, the University of Nebraska and Northwestern University. He also lectured on the Carolina Craters at Clark University and on "Geology and Strategy in the Present War" at Indiana University, the Rice Institute, the University of Nebraska, Northwestern University and also at the University of Kansas, where he gave a second lecture entitled "Is the Atlantic Coast Sinking?"

THE fourth International Congress of Malaria will be held in Rome on the occasion of the International Exhibition of 1942.

THE annual meeting of the American Pharmaceutical Association will be held in Richmond from May 5 to 11. The association will meet in sections, including: a Scientific Section; a Section on Practical Pharmacy and Dispensing; a Section on Historical Pharmacy; a Section on Education and Legislation, and a Section on Economics. The American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy and the Plant Science Seminar will also meet in Richmond during the week.

MEMBERS and guests of the Sigma Xi Club of Hawaii met at the University of Hawaii on the evening of March 25 to hear a symposium on "Progress in Plant Breeding in Hawaii," a discussion of the advances in Hawaiian agriculture made possible by the application of the principles of genetics. The speakers were Dr. J. L. Collins, geneticist, Experiment Station of the Pineapple Producers Cooperative Association; Dr. A. J. Mangelsdorf, geneticist, Experiment Station of the Hawaiian Sugar Planters' Association, and Dr. J. H. Beaumont, director and horticulturist, Hawaii Agricultural Experiment Station.

DR. EDWARD WIGGLESWORTH, scientific director of the New England Museum of Natural History, has arranged an exhibit of synthetic and genuine gems, and described on April 10 before the American Academy of Arts and Sciences the methods in use for identifying synthetic cut gems, demonstrating the method with the aid of "Diamondscopes."

DISCUSSION

A CHYTRID IN RELATION TO CHLOROTIC STREAK DISEASE OF SUGAR-CANE

CHLOROTIC streak, a systemic disease of sugar-cane occurring in Java, Hawaii, Queensland, Puerto Rico and Louisiana, is characterized by the variable development of one or more yellowish streaks on the leaves. The streaks follow the veins, are more or less diffuse in outline, often discontinuous, and may not extend to either midrib or edge of leaf. The lesions often become necrotic. A red discoloration of the vascular bundles in the nodes is also a variable symptom. Vague, evanescent symptoms and latency are typical. The effects of the disease are poor germination of cuttings, depressed growth and the development of stalks of less than normal size. The disease in severe form is sharply restricted to wet localities. Uniformly negative results have attended investigations to find a causal agent of this obscure disease.

Recently a primordial fungus with affinities in the Chytridiales has been found to be a frequent invader of the cells of the leaves, stalks and buds of sugar-cane affected with chlorotic streak disease. It has been observed in several varieties of cane collected from several islands of the Territory of Hawaii. In apparently healthy cane it has been found only where latent infection presumably existed. For convenience this fungus is tentatively referred to as a chytrid.

The chytrid in its most conspicuous form may be seen in longitudinal sections of the nodal region of the stalk with a hand lens at a magnification of 10 as an assortment of black spheres of various sizes. Under the compound microscope these spheres were found to range in size from about 5 microns to 60 microns, the smaller spheres being of the color and density of the host cell protoplasm, slightly larger ones gray, and the larger units opaque and black even with high magnification and intense illumination. The naked thallus of the fungus was observed in the same cells with one or more of the spherical bodies. The thallus is often attenuated into scarcely discernible strands with enlargements, resembling those of *Physoderma zeae maydis* Shaw, disposed at intervals on the inner surface of the host cell walls. Apparently the thallus may also assume the form of rounded or amoeboid bodies as well as attenuated masses of naked protoplasm elsewhere in the plant where it is more active, in the absence of the spherical bodies. Wherever observed the thallus was predominantly intracellular. It often contains black inclusions which serve to identify it where otherwise it would be undetected since the naked protoplasm of the invader is almost entirely lacking in contrast with the host cell protoplasm.

This chytrid apparently has heretofore escaped observation by sugar-cane pathologists, which may largely be attributed to the occurrence of the conspicuous phase of the fungus in tissues difficult to section, and to the longitudinal rather than radial distribution of the invading thallus.

A preliminary report concerning observations which indicate that the above-mentioned chytrid may be the causal agent of chlorotic streak disease, with photographs of the several stages of the fungus, was submitted February 19, 1940, for publication in *The Hawaiian Planters' Record.*

C. W. CARPENTER

EXPERIMENT STATION OF THE
HAWAIIAN SUGAR PLANTERS' ASSOCIATION

THE GENUS LISTERELLA PIRIE

I HAVE been informed that at the Third International Congress for Microbiologists, held in New York City, September 2–9, 1939, it was reported to the Committee on Nomenclature that the new name *Listerella* which I proposed for a genus of bacteria in 1927 had already been given to a Mycetozoan by Jahn[1] in 1906 and to one of the Foraminifera by Cushman[2] in 1939.

My proposed name, therefore, becomes a homonym, but as the genus has acquired some importance in both human and veterinary pathology and references to "Listerellosis" are becoming fairly common in literature, I think that a name as near to my original proposal as possible is desirable. I therefore propose *Listeria,* as the name for the genus of bacteria as defined by me in Publication No. XX of the South African Institute for Medical Research.[3] The type species of this genus is *Listeria monocytogenes* (Murray *et al.*) comb. nov. *Bacterium monocytogenes* Murray, Webb and Swann;[4] *Listerella hepatolytica* Pirie.[5]

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SCIENTIFIC CONSCIENCE

IN two of the recent numbers of SCIENCE, Professor Ashley-Montagu has pointed out how two early writers (Leonardo da Vinci and Francesco Lanza Terzi), both pioneers, exhibited fear that inventions with which they were concerned might be used for the destruction of mankind, rather than its preservation.[1] In this light it is interesting to note what Benjamin Franklin had to say on the subject.

Franklin had been present at the balloon ascents of Montgolfier and Charles and had written from Paris detailed accounts of these ascents to Sir Joseph Banks, the president of the Royal Society. In a letter to his friend Jan Ingenhousz—the physician to Maria Theresa—dated January 16, 1784, he wrote:

> It appears, as you observe, to be a discovery of great Importance, and what may possibly give a new turn to human Affairs. Convincing Sovereigns of the Folly of wars may perhaps be one Effect of it; since it will be impracticable for the most potent of them to guard his Dominions. Five thousand Balloons, capable of raising two Men each, could not cost more than Five Ships of the Line; and where is the Prince who can afford so to cover his Country with Troops for its Defence, as that Ten Thousand Men descending from the Clouds might not in many places do an infinite deal of mischief, before a Force could be brought together to repel them?[2]

Franklin's abhorrence of wars is well expressed in

[1] *Ber. d. deutsch. Bot. Ges.,* Vol. 23, p. 538.
[2] "Foraminifera, Their Classification and Economic Use," Sharon, Mass., p. 122, plate 12, fig. 13.
[3] "The Plague Problem in South Africa," by J. A. Mitchell, J. H. Harvey Pirie and A. Ingram, (Whole Vol. III, 1927, p. 169.
[4] *Jour. Path. and Bact.,* 29: 1926, 407.
[5] *Publ. S. African Institute for Med. Res.,* 3: 1927, 163.
[1] SCIENCE, 90: 180, 1939; and 90: 592, 1939.
[2] "The Writings of Benjamin Franklin," edited by A. H. Smyth, New York, 1907. Vol. ix, Letter 1473, p. 155.

another letter to Ingenhousz, dated February 11, 1788, in which he said:

I lament with you the Prospect of a horrid War, which is likely to engage So great a Part of Mankind. There is little Good gain'd, and so much mischief done generally, by Wars, that I wish the Imprudence of undertaking them was more evident to Princes; in which case I think they would be less frequent.[3]

I BERNARD COHEN

CARNEGIE INSTITUTION
OF WASHINGTON

"ROGER BACON WAS MISTAKEN"

IN SCIENCE of March 29, I find an article entitled "Roger Bacon Was Mistaken," in which the author attributes to Roger Bacon the statement that "hot water would freeze more quickly than cold water."

The present writer is not an authority on the writings of Roger Bacon, though he has given some attention to them, and he has no recollection of seeing any discussion of temperature changes in Roger Bacon's writings; but he is aware that some four hundred years later Francis Bacon devoted a considerable portion of his "Novum Organum" to a discussion of "The Form of Heat." In this discussion he says:

The preparation of bodies, also, for the reception of cold should not be omitted, such as that water a little warmed is much more easily frozen than that which is quite cold, and the like.

In his "Table of the Degree or Comparative Instances of Heat" he says in example 39:

A brick or stone or hot iron, plunged in a basin of cold water and kept there for a quarter of an hour or thereabouts, retains such a heat as not to admit of being touched.

Evidently, Lord Bacon in this case must have performed his critical experiment in the same manner as did the author of the article on Roger Bacon's mistake. In this latter instance it would be very interesting to know why the pint of water from mother's tea-kettle continued to cool faster than the pint from the kitchen faucet after they had both reached the same temperature.

FERNANDO SANFORD

STANFORD UNIVERSITY

PROFESSOR JOSEPH O. THOMPSON'S comments on the freezing of hot water sooner than cold water appealed to me rather keenly. When I was a schoolboy some of my elders said that the hot water pipes always froze first and that hot water, put in a vessel and exposed to the atmosphere, would freeze more quickly than cold water placed in a similar vessel. The idea appeared so preposterous to me that I performed exactly the experiment performed by Bacon. I got two deep pans of the same shape and size. One I filled with cold water and the other with hot water, placed them on a cold porch one evening and watched the rapidity with which each froze. I was pleased to note that the one containing cold water froze very much sooner than the one containing hot water, much to the disgust of my elders.

If Professor Thompson's volume of water which had been heated becomes rapidly less in volume than the cold water, the experiment does not seem to be carried out along strictly scientific lines.

The belief that hot water does freeze more quickly seems to be firmly ingrained in the public mind so that many persons believe if hot water is placed in the ice-cube compartment of an electric refrigerator it will freeze faster than if cold water is placed therein. Perhaps it will if a large portion of it is lost through evaporation.

M. W. LYON, JR.

SOUTH BEND, IND.

BEING mildly intrigued by Dr. J. O. Thompson's recent note: "Roger Bacon Was Mistaken,"[1] I repeated the experiment at Caribou, Colo. (elevation, 10,600 feet) on an evening during which the temperature fell from −14° C. to −17° C.

Four 500 cc glass cylinders and four ordinary pie-tins were used in the experiment. These were placed on the wooden floor of the cabin-porch. The volume of water used in each case was very nearly 250 cc. Twin-samples of water at various temperatures were placed in cylinders and pie-tins—and the times recorded for the first appearance of ice crystals. The results are given in the table:

Type of receptacle	Original temperature of water	Time of cooling to freezing point
Cylinder	93.3° C.	54 min.
Pie-tin	93.3° C.	31 "
Cylinder	30° C.	42 "
Pie-tin	30° C.	33 "
Cylinder	20° C.	39 "
Pie-tin	20° C.	31 "
Cylinder	10° C.	37 "
Pie-tin	10° C.	29 "

Perhaps it should be noted that at an altitude of 10,600 feet brook-water boils at 93.3° C. Slightly different results might have been obtained with distilled water at sea-level.

Only in one case did the originally boiling water freeze, (in a receptacle of the same type), more quickly than cold water, and even in this case the "cold" water was nearly lukewarm. It seems clear that the shape and heat-capacity of the receptacle are critical. Various other factors may be involved.

[3] *Ibidem*, Letter 1715, p. 633.

[1] SCIENCE, 91: 2361, 315, March 29, 1940.

Roger Bacon and the "ancients" were probably both right in so far as they reported the results of individual experiments. They were both wrong in generalizing from insufficient experimental data. I do not presume to say what Dr. Thompson was.

UNIVERSITY OF COLORADO G. WAKEHAM

SCIENTIFIC BOOKS

THE THEORY OF NUMBERS

Modern Elementary Theory of Numbers. By LEONARD EUGENE DICKSON. vii + 309 pp. Chicago: The University of Chicago Press. 1939.

THIS book provides an account of the essentials of the classical theory of numbers, and of such special topics as Diophantine equations of the second degree, the representation of integers by quadratic forms in three or more variables (with integer coefficients and variables), Waring's problem for cubes and fourth powers, and other problems of representation by quadratic, cubic or quartic polynomials, in so far as these questions can be handled by elementary (*i.e.*, non-analytical) methods.

The word "modern" in the title is justified by the inclusion of new or recent results and methods, due in the main to the author and his pupils. Thus the theorem that every positive integer can be expressed as a sum of nine non-negative integral cubes (the classical solution by Wieferich and Kempner of the "universal" Waring's problem for cubes) is treated as a particular case of representation by $\sum_{i=1}^{9} h_i x_i^3$ (where the h_i are assigned positive integers and the variables x_i are restricted to non-negative integer values), and the author gives an extensive list of cases in which this form is "universal," *i.e.*, represents all positive integers. As another extension of Waring's problem for cubes the representation of positive integers by $\sum_{i=1}^{9} \varphi(x_i)$ is discussed for various integer-valued cubic polynomials $\varphi(x)$. Wieferich's theorem that every positive integer can be expressed as a sum of 37 positive or zero fourth powers (the nearest approach by elementary methods to the 19 which is believed to be the "correct" number) is proved by a method which shows in addition that 20 of the 37 fourth powers can be taken equal in pairs.

The sections on quadratic forms include a discussion of "universal" forms (*i.e.*, positive definite or indefinite forms which represent all positive integers or all integers respectfully), and of "zero forms" (*i.e.*, indefinite forms which represent the number zero with integer values of the variables not all zero).

An appendix is devoted to Dirichlet's theorem on primes in an arithmetical progression, a result frequently required though not "elementary" in the strictest sense.

It may perhaps be felt that the scope of the book hardly justifies so comprehensive a title, for the elementary theory of numbers has made important advances in other directions in recent years. A notable example is the additive theory of the "density" of sequences of integers, created in the last decade. Within its own limits, however, the book is a storehouse of information on a variety of topics not easily accessible hitherto, and the author has made the proofs about as simple as can be expected from the nature of the problems. This is not to say that the book will be found easy reading by anyone who sets out to work conscientiously through its 309 compactly written pages of text and examples (some of which are quoted in the text), for many of the discussions necessarily involve much intricate detail and lengthy enumeration of cases. The reader interested in a particular topic can, however, read selectively; and the reader desiring to pursue any subject further will find the essential references scattered through the text.

A. E. INGHAM

UNIVERSITY OF CAMBRIDGE

A MATHEMATICAL CLASSIC

Topological Groups. By L. PONTRJAGIN (translated by Emma Lehmer). ix + 299 pp. Princeton, 1939.

PROFESSOR PONTRJAGIN'S book on "Topological Groups" is more than distinguished; it is a mathematical classic. The subject of topological algebra, occurring as it does at the junction of two great streams of thought, has been one of the most fascinating mathematical developments of the past fifteen years. The present volume by the brilliant blind Russian scientist is likely to remain far and away the most important work on this subject for many years to come.

The main theme of the book is the "analyticity" and representability by ordinary matrices of compact and (locally compact) commutative topological groups. One's enjoyment of the beautifully clear exposition of this theme is enhanced by the realization that many of the principal ideas are due directly to the author. The discussion is also rounded off at the end by an appropriate selection of related special topics from the theory of Lie groups.

Although the book generalizes a theory which has proved of great importance in quantum mechanics, it is probably too abstract and technical for the non-mathematician. But it should be an ideal text for graduate courses in mathematics, both because of the value of the contents and as an introduction to modern mathematical ideas.

GARRETT BIRKHOFF

REPORTS

THE ENGINEERING FOUNDATION

SEVENTY-THREE research projects involving an aggregate of $3,111,374 have been carried out by The Engineering Foundation since it was established in 1914 by Ambrose Swasey, the Cleveland manufacturer, "for the furtherance of research in science and engineering or for the advancement in any other manner of the profession of engineering and the good of mankind."

Notable contributions have been made to science, engineering, industry and the humanities during a twenty-five-year period characterized by profound change, according to a report made public by Dr. Otis E. Hovey, director of the foundation, in which it is stated that the opportunities for productive research are constantly increasing in number and scope.

"Researches have been assisted by funds appropriated from the income of the investments of the foundation to an amount of over $400,000. Cash contributions for certain projects have passed through the accounts of the foundation to an amount of nearly $500,000.

"In addition, other large sums have been contributed by the four founder societies of civil, mining and metallurgical, mechanical and electrical engineers and by individuals, corporations and industry. Likewise, the use of facilities made available by educational institutions and laboratories, and the expert supervision freely donated by many individuals have been of great value, but a large part of such service can not be expressed in an equivalent money value."

A ten-year research in the field of alloys of iron representing, in cash contributions and service, an outlay of $426,677 was among the chief activities. With the cooperation of eighty-eight manufacturers, research institutes, technical societies and federal bureaus, hitherto inaccessible world knowledge of steel and iron and their alloys has been assembled from scientific and technical literature of many nations. The results have been embodied in eleven monographs by a committee of which Professor George B. Waterhouse, of the Massachusetts Institute of Technology, representing the American Institute of Mining and Metallurgical Engineers, is chairman and director.

Dr. John Johnston, director of research of the United States Steel Corporation, says in this section of the report that "the justification for this undertaking is that by showing what is still uncertain and unknown, it provides a new starting point for supplying the engineer with the metal best fitted for each of his multifarious purposes."

Another research aided by the foundation is proceeding under the sponsorship of the special research committee on cottonseed processing of the American Society of Mechanical Engineers in the laboratory of the University of Tennessee, with the cooperation of the Tennessee Valley Authority. Large contributions of money, materials and services have been made as the work progressed, and the data developed give promise of large returns to the industry and the public. "A number of plants are now operating in America on the basis of new discoveries resulting from this research," Dean W. R. Woolrich, of the University of Texas, chairman of the committee, says in describing the work at the University of Tennessee. "The mechanical processing of cottonseed has been improved to a much higher degree of perfection—an improvement in this art that is most outstanding since the beginning of the twentieth century."

The results of an arch dam investigation, which included the building of an experimental dam on Stevenson Creek, about sixty miles east of Fresno, Calif., "have had a far-reaching influence on the design of dams, both arch and gravity," according to the report. The investigation developed instruments and methods of test which have been employed in practically all dams of recent construction.

Research in the fatigue of metals, sponsored by the foundation and the National Research Council, were carried out at the University of Illinois under the direction of Professor H. F. Moore. "The results of this work have been far-reaching, not only with respect to the factual data developed but in the stimulation of similar research work in the United States and several other countries. The work stands as the first of the later researches on fatigue phenomena, and has contributed greatly to our knowledge of the endurance characteristics of some of the most commonly used of the structural metals."

Other foundation researches which have contributed to the progress of science, engineering and industry embraced welding, personnel research, concrete and reinforced concrete arches, steel columns, earths and foundations, plastic flow of concrete, hydraulics, mining methods, blast furnace slags, barodynamics, thermal properties of steam, lubrication, fluid flow, effect of temperature on properties of metals, cutting metals, plasticity of metals, dielectric absorption and engineering education.

Ambrose Swasey made five gifts to the foundation amounting to $818,600. Gifts by Edward Dean Adams, Henry R. Towne, W. S. Barstow and Sophie M. Gondron amount to $131,600, and nine others have given $29,600. The book value of the endowment fund is given as $990,000. A bequest by E. H. McHenry, in the hands of executors during the life of two beneficiaries, was appraised in 1931 at $400,000.

"The purpose and scope of the foundation are broad,

and it was the hope of the founder that his gift would be the nucleus of a large endowment fund contributed by many persons and many organizations, thus making available ample income to support worth-while investigations which would advance science, the profession of engineering and the good of mankind."

The following general policy has been adopted by the Engineering Foundation Board: "The Foundation will concern itself with human as well as technical aspects of engineering problems of wide interest. Activities which will have as their main objectives 'the advancement of the profession of engineering,' whether by research or other means, will be given preference. The foundation will initiate new projects or will select from time to time projects presented to it which are deemed most likely to attain its objectives."

SPECIAL ARTICLES

ANTHELMINTIC ACTIVITY OF CRYSTALLINE PAPAIN

The anthelmintic properties of certain plant extracts were recognized and made use of by some physicians as early as 1802, but the use of such extracts seems to have been neglected in recent years. Possible reasons for this were the inconvenience of handling the relatively unstable fresh juices and the ignorance of the fact that the anthelmintic properties were associated with labile enzymes. It was reported in 1802,[1] 1879[2] and 1881[3] that many physicians had successfully used the crude latex of *Carica papaya* or the papain obtained from it against ascarids, tapeworms, trichuris and hookworm lodged in the intestinal canal. The effectiveness of the enzyme was demonstrated beyond doubt. Although the anthelmintic value of ficin has been reinvestigated recently,[4, 5] the use of papain appears to have been completely forgotten. That large amounts of dried preparations of this enzyme are available is shown by the fact that in 1938 the United States imported 222,675 pounds of papain, according to the Chemical Division, Department of Commerce.

The present authors have reported[6] that bromelin of fresh pineapple juice can digest live Ascaris worms *in vitro*. In a search for other active plant proteases, it was found that a commercial preparation of papain (Merck) possessed strong worm-digesting activity. This finding is a confirmation of certain claims made in 1879.[2] A 0.7 per cent. solution of dried preparation in M/18 phosphate-phthalate buffer pH 5 digested *Ascaris lumbricoides* (obtained from hog intestines) almost completely in 17 hours, while a 0.07 per cent. solution also showed some activity. Since this preparation had been on hand several years, a fresh sample was analyzed and found to have approximately the same activity. *Macracanthorynchus hirudinaceus* (from hog intestine) was not digested by a 0.7 per cent. solution of either of these papain preparations, but was digested by fresh pineapple juice.[7]

It has frequently been suggested[8] that crude papain contains more than a single protease. It was therefore desirable to determine whether the worm-digesting activity of crude papain was attributable to papain itself or to some accompanying enzyme. To settle this question, pure crystalline papain[9] was tested on *Ascaris lumbricoides*. As may be seen from Table 1, rapid ulceration, followed by digestion of worm tissue, occurred in tubes containing 0.11 per cent. of crystalline papain, while digestion took place more slowly in weaker concentrations of enzyme. The crystalline enzyme was 14 times as active as the commercial preparations in worm-digesting ability.

TABLE 1

WORM-DIGESTING ACTIVITY OF CRYSTALLINE PAPAIN

Concentration of enzyme[1]	Observations on worms after		
	2 hours	7 hours	16 hours
Per cent.			
0	No change	No change	No change
0.005	" "	1 worm ulcerated, other 2 unaffected.	2 worms ulcerated, other unaffected.
0.02	" "	6–12 ulcers per worm.	All 3 worms badly ulcerated and partly digested.
0.11	Numerous ulcers on 3 worms; some digestion begun.	Worms badly ulcerated and partly digested.	All 3 worms completely disintegrated and well-digested.

[1] The enzyme was dissolved in 12.5 cc of 0.067 M phosphate-phthalate buffer, pH 5. One worm was placed in each test-tube (15 x 150 mm.) and the tube incubated at 40° C. All determinations were made in triplicate. The enzyme crystals had an activity of 11 units per mg. of protein N, determined by milk clotting (private communication from Dr. A. K. Balls).

Walti[5] has reported that crystalline ficin can also digest live ascarids *in vitro*. It therefore appears that the anthelmintic properties of the latex of Ficus spe-

[1] R. Sprengel, *Medicinisch chirurgische Zeitung*, 1: 353, 1802.

[2] A. Wurtz and E. Bouchut, *Paris Médical*, pp. 5–35, 1879.

[3] Anonymous, *Paris Médical*, No. 30, July 28, 1881.

[4] F. C. Caldwell and F. L. Caldwell, *Am. Jour. Trop. Med.*, 9: 471, 1929.

[5] A. Walti, *Jour. Amer. Chem. Soc.*, 60: 493, 1938.

[6] J. Berger and C. F. Asenjo, SCIENCE, 90: 299, 1939.

[7] Puerto Rican pineapples were used here.

[8] A. K. Balls and H. Lineweaver, *Jour. Biol. Chem.*, 130: 669, 1939.

[9] The authors are particularly grateful to Dr. A. K. Balls, of the United States Department of Agriculture, for a generous gift of crystalline papain.

cies and of *Carica papaya* are to be attributed to the proteinases of these plants. However, there is some evidence on hand that certain other plant proteinases which are as proteolytically active as papain do not possess this peculiar ability to digest live worms.

JULIUS BERGER
CONRADO F. ASENJO[10]

UNIVERSITY OF WISCONSIN

CONVERSION OF ESTRADIOL TO ESTRONE IN VIVO[1,2]

WESTERFELD and Doisy measured the estrogenic activity of the phenolic fraction of the urine of monkeys injected with estradiol.[3] They found that 30 to 45 per cent. of the activity of the excreted estrogens was present in the ketonic fraction. After the administration of estradiol to estrous, hysterectomized estrous, or pregnant rabbits, Pincus showed the possible presence of estrone in the urine.[4] He was unable, however, to find any evidence for estrone in the urine of ovariectomized animals injected with estradiol. Neither the work of Westerfeld and Doisy nor that of Pincus was supported by chemical isolation and identification of metabolic products. This communication deals with the isolation and identification of estrone from the urine of long-time ovariectomized guinea pigs to which estradiol had been administered.

Ten mg of estradiol dipropionate in oil solution were administered by subcutaneous injection daily for 5 days to each of 5 adult guinea pigs which had been ovariectomized for at least one year. The urine was quantitatively collected during the injection period and for the following 5 days. After acidification with 10 per cent. of concentrated hydrochloric acid, the mixture was refluxed for 15 minutes and thoroughly extracted with benzene. That portion of the extract representing the phenolic compounds was separated by the Girard-Sandulesco reagent into ketonic and non-ketonic fractions.

The ketonic fraction contained more than 50,000 I. U. of estrogenic material when assayed by the vaginal smear test on the spayed adult mouse. The ketonic substances were subjected to high vacuum sublimation and the fraction subliming at 150° C. and 3 micra of mercury was collected. This semicrystalline material was crystallized from methanol and a crop of approximately 5 mg of crystals, m. p. 242–245° C., was recovered. After recrystallization from methanol, the melting-point was raised to 245–246° C. The melting-point of a mixture of this compound with an authentic sample of estrone (m. p. 255–258° C.) was 247–249° C. The benzoate melted at 211–214° C. When mixed with a sample of estrone benzoate (m. p. 215–217° C.), the melting-point was 211–214° C. All melting-points are uncorrected.

In a second experiment 50 mg of estradiol dipropionate were administered orally for 2 days to each of 5 adult guinea pigs spayed for at least one year. A procedure similar to that outlined above was used with the following modification: The phenolic compounds were fractionated between 0.1 N sodium hydroxide and 10 per cent. sodium hydroxide and the material soluble in the latter solvent separated into ketonic and non-ketonic portions by the Girard-Sandulesco reagent. About 12 mg of crystalline estrone, m. p. 256–257° C., were obtained from the ketonic fraction without resorting to high vacuum sublimation. It did not depress the melting-point of an authentic sample of estrone.

Thus it appears from this work that, at least in the guinea pig, estradiol may be converted to estrone even in the absence of the ovary. This and further work on the metabolism of the estrogenic hormones will be reported in detail.

We are indebted to Ciba Pharmaceutical Products, Inc., for the supply of estradiol dipropionate and estrone benzoate, and to the Schering Corporation for estrone.

WILLIAM R. FISH
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TOMATO POMACE IN THE DIET

TOMATO pomace is the term applied to the dried residues that remain after the preparation of tomato juice. These residues contain the seeds, skin and some of the original pulp. The composition of the material used in our studies was the following: Protein, 24 per cent.; ether soluble, 14 per cent.; fiber, 33 per cent.; ash, 4 per cent., and moisture, 7 per cent. An analysis for pectin by Z. I. Kertesz, of Geneva, N. Y., showed 3.8 per cent. of this substance.

Three properties of this tomato pomace attracted our attention while improved feeding mixtures were being developed for dogs, foxes and minks. A sample of tomato pomace was ground for a rat assay and for a carotene determination. After these were made the material was left in a mason jar without a rubber for a year in a warm laboratory. At the end of this time

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[1] This work was supported by grants from the Committee for Research in Problems of Sex, National Research Council: Grant administered by Dr. William C. Young; by the Rockefeller Foundation, and by the Fluid Research Fund of Yale University School of Medicine.

[2] From the Laboratories of Physiological Chemistry and Primate Biology and the Adolescence Study Unit, Yale University School of Medicine, New Haven.

[3] W. W. Westerfeld and E. A. Doisy, *Ann. Int. Med.*, 11: 267, 1937.

[4] G. Pincus, *Cold Spring Harbor Symposia on Quant. Biol.*, 5: 44, 1937.

[1] C. M. McCay, "The Nutritional Requirements of Dogs," p. 27. Ithaca, 1939.

t was assayed and the carotene determined again. Much to our surprise there was little decrease in the carotene content and in both cases the rat needed about 100 mg daily when this was the only source of vitamin A. This level, which is roughly 1 per cent. of the diet, permits a weekly gain of about 16 gm.

Furthermore, at the end of the year there was no evidence of rancidity either by taste or by the usual color tests such as the Kreis' one. Mattill and co-workers found antioxydants in tomato oil some time ago. There is a belief among some dog-feed manufacturers that dogs prefer freshly ground tomato pomace, but this has not been proved by rigid tests.

In the course of feeding diets that are relatively rich in carbohydrates to dogs, it is usual to observe periods of soft feces that may contain enough water at times to be considered a condition of diarrhea. While feeding a group of dogs a diet containing 5 per cent. of tomato pulp, the senior author observed unusual uniformity in fecal composition during a period of three months. When the tomato pulp was decreased to half this amount the uniformity in the fecal composition persisted. Subsequent observations with dogs have confirmed our earlier ones. Tomato pomace is being used in a number of dry dog feeds.

Nutritional studies of foxes and minks are being made by the junior author, and some of the experimental diets were causing loose feces that were entirely lacking in form. In some cases the looseness bordered on a diarrhea. It was found that by adding to the diet a quantity of ground, dried tomato pomace equal to 5 per cent. of the wet ration, the fecal form would change rapidly. In some instances the feces assumed good form and consistency within a day after the addition of the pomace to the diet and remained in good form as long as it was included. If the tomato pomace were excluded from the diet, the feces again returned to a loose condition. Tomato pomace contains carotenoids, and these were objectionable for diets planned to study vitamin A deficiency. For these diets the pomace was extracted for forty-eight hours with 95 per cent. ethyl alcohol to remove the carotenoids. This alcohol extraction did not affect the pomace so far as its desirable effects on the feces were concerned.

These observations have been reported at this time since they may have some use in both human and animal nutrition.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE PREPARATION OF PURIFIED HOUSE-DUST EXTRACTS

HOUSE dust is a frequent cause of allergic symptoms such as asthma and hay-fever. In common with other allergic extracts, house-dust extracts prepared by the usual method of simple extraction with aqueous extracting fluids contain a relatively large amount of material other than the allergically active substance. We are able to report at this time the preparation of highly purified, highly concentrated extracts which we have been able to show are allergically more active than house-dust extracts prepared by the methods in use previous to this work. House-dust extracts prepared by our technique uniformly produce strong positive scratch-test reactions in house-dust sensitive individuals.

For the purification of house-dust extracts, aqueous extracts of house dust were subjected to fractional precipitation by the addition of water-miscible organic solvents such as acetone, dioxane and isopropanol. The technique of the fractional precipitation may be described briefly as follows: The precipitate which formed when a small amount of the organic liquid was added to the original extract was removed, and then an additional amount of the organic liquid was added to the filtrate; this procedure was repeated to give progressively larger proportions of organic liquid with successive separations of insoluble fractions. In this manner the mixture of solids constituting the solute of the original house-dust extract was separated into a number of fractions.

Comparative skin tests[1] performed with solutions of the various fractions showed that the fractions precipitated by lower concentrations of the organic liquids, as well as those precipitated by concentrations of organic liquids above 75 per cent. were relatively allergically inert; the fraction precipitated by the intermediate concentrations of organic liquids possessed marked allergic activity.

This active fraction could be further purified by subjecting it to refractionation with the same or with a different organic liquid. Repeated refractionation of the purified active fraction resulted in no further separation of allergically inert material.

A greater degree of purification was obtained by subjecting the fractionated and refractionated extract to dialysis through number 1200 Cellophane membranes.

Extracts purified by fractionation with organic

[2] Agent in U. S. Bureaus of Biological Survey and Animal Industry.

[1] C. H. Boatner, M. R. Pabst and B. G. Efron, "Analysis of Comparative Skin Tests." To be published.

liquids and dialysis contained a greater degree of skin-reacting activity per unit of dissolved material than did the original extracts from which the purified extracts were processed.

The extract purified by fractionation and refractionation with organic liquids was further purified by treating it with high concentrations of soluble sulfates such as ammonium sulfate, sodium sulfate and zinc sulfate. The fraction precipitated from concentrated solutions of these sulfate salts contains a very high degree of specific allergic activity. It produces uniformly strong positive scratch-test reactions in house-dust sensitive individuals in concentrations of 0.5 per cent.; specific intracutaneous tests are obtained with this extract in dilutions of 1/50,000 to 1/5,000,000.

Chemical analysis of all the fractions, the allergically active as well as the allergically inert, failed to show any significant difference in nitrogen or reducing sugar content.

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A LABOR-SAVING TECHNIQUE FOR LEAF SAMPLES IN HISTOLOGICAL WORK

IN the course of various studies on plant leaves it is often necessary to employ extensive sampling for histological material. The resulting collection of samples may come from various parts of the same leaf or from similar portions of different leaves. In either case the accurate recording of the source of each sample, as well as the maintenance of its identity throughout the stages in its preparation and storage before sectioning, is greatly facilitated by the use of India ink index numbers on the sample itself and upon the portion of leaf adjacent to it. The latter is then pressed, dried and kept as a record of the sample origin, or left in its original position on the plant when further samples are to be collected at a later stage in the development of the same leaf.

The general procedure is as follows: Duplicate numbers in India ink are put on the fresh leaves in the region from which the sample is to be taken. (Higgins waterproof black American India ink was used with satisfactory results.) A disc-shaped portion of the leaf including one of these numbers is punched out to furnish the sample, and the other number is left to record its source. A crow-quill pen is most satisfactory for producing small numbers without injury to the leaf tissues. With a clean pen no difficulty is encountered in numbering the leaves provided their surface is free of water. Care must be taken, however, that no pressure is applied by the pen to the tissues beneath, and that the numbers are dry before the samples are placed in the fixing fluid.

Following this technique the writer has fixed and preserved as many as fifteen leaf samples, each ¼ inch in diameter, in a single 4-dram vial. The use of fourteen vials, index tabs and record entries in each group of fifteen samples was thus avoided. These sections can in turn be carried through dehydration and embedding as a unit, further avoiding fourteen out of every fifteen separate operations that would otherwise be necessary in these steps. In the process of embedding, the tissue samples are arranged in the warm paraffin so that they do not overlap one another, and so that the sides of the samples bearing the numbers face the lower side of the block, being thus legible through the thin paraffin layer. The resulting single paraffin block containing all the samples from a given leaf or plant has been found most convenient for storage and record-keeping purposes until sectioning is begun. Pressed and dried shoots bearing the leaves from which the samples were punched furnished a simple but excellent record of the sample origin.

The ink numbers are not dissolved or faded by chrom-acetic or by formalin-acetic-alcohol fixatives, or by any grade of alcohol in the ethyl or butyl alcohol series. The numbers withstand equally well the treatment of the samples with such clearing agents as dioxan and chloral hydrate. The numbered samples are clearly visible in the paraffin block permitting the ready location of any one of them desired for sectioning. The occasional necessity of sectioning directly through the numbers does not impose any restriction on the use of the technique.

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